CLAIMS

1. A method for treating a disease with a tetracycline compound having a target therapeutic activity, comprising administering to a subject an effective amount of a tetracycline compound having said target therapeutic activity, such that the disease is treated.

2. The method of claim 1, wherein said disease is an inflammatory process associated state.

3. The method of claim 2, wherein said inflammatory process associated state is acute lung injury, adult respiratory distress syndrome, acute respiratory distress syndrome, aortic or vascular aneurysms, arteriosclerosis, atherosclerosis, bone or cartilage degradation, bronchiectasis, cancer, chronic obstructive pulmonary disease, corneal ulceration, cystic fibrosis, diabetes, diabetic complications, diabetic ulcers, dry eye, emphysema, ischemia, restenosis, malaria, metastasis, multiple sclerosis, osteoarthritis, osteoporosis, osteosarcoma, osteomyelitis, periodontitis, rheumatoid arthritis, neurological disorders, senescence, skin and eye diseases, stroke, tissue wounds, tumor growth, tumor invasion, ulcerative colitis, or vascular stroke.

4. The method of claim 2 or 3, wherein said inflammatory process associated state is associated with a matrix metalloproteinase.

5. The method of claim 4, wherein said matrix metalloproteinase is MMP-1, MMP-2, MMP-3, MMP-4, MMP-5, MMP-6, MMP-7, MMP-8, MMP-9, MMP-10, MMP-11, MMP-12, MMP-13, MMP-14, MMP-15, MMP-16, MMP-17, MMP-18, MMP-19 or MMP-20.

6. The method of claim 2, wherein said inflammatory process associated state is a NO associated state.

7. The method of claim 2, wherein said inflammatory process associated state is a chronic or recurrent inflammatory disorder.

8. The method of claim 2, wherein said inflammatory process associated state is an acute inflammatory disorder.

9. The method of claim 3, wherein said inflammatory process associated state is diabetes.

10. The method of claim 9, wherein said diabetes is juvenile diabetes.

11. The method of claim 9, wherein said diabetes is diabetes mellitus.

12. The method of claim 9, wherein said tetracycline compound inhibits protein glycosylation in said subject.

13. The method of claim 3, wherein said inflammatory process associated state is rheumatoid arthritis or osteoarthritis.

14. The method of claim 2, wherein disease is a bone mass disorder.

15. The method of claim 14, wherein said bone mass disorder is osteoporosis.

16. The method of claim 3, wherein inflammatory process associated state is a vascular aneurysm of vascular tissue.

17. The method of claim 16, wherein said tetracycline compound prevents the formation of said vascular aneurysm.

18. The method of claim 16, wherein said tetracycline compound induces the regression of said vascular aneurysm.

19. The method of claim 16, wherein said vascular tissue is an artery of said subject.

20. The method of claim 3, wherein said disease is acute respiratory distress syndrome (ARDS).

21. The method of claim 3, wherein said disease is a tissue wound.

22. The method of claim 3, wherein said disease is ischemia or stroke.

23. The method of claim 3, wherein said disease is dry eye.

24. The method of claim 2, wherein said disease is an acute, chronic or recurrent lung disorder.

25. The method of claim 24, wherein said chronic lung disorder is asthma, emphysema, bronchitis, or cystic fibrosis.

26. The method of claim 2, wherein said disease is hepatitis or sinusitis.

27. The method of claim 3, wherein said disease is diabetic complications or diabetic ulcers.

28. The method of claim 1, wherein said disease is a neurological disorder.

29. The method of claim 28, wherein said neurological disorder is Alzheimer's disease, a dementia related to Alzheimer's disease, Parkinson's disease, Lewy diffuse body disease, senile dementia, Huntington's disease, Gilles de la Tourette's syndrome, multiple sclerosis, amylotropic lateral sclerosis (ALS), progressive supranuclear palsy, epilepsy, Creutzfeldt-Jakob disease, an autonomic function disorder, hypertension, a sleep disorder, a neuropsychiatric disorder, depression, schizophrenia, schizoaffective disorder, Korsakoff's psychosis, mania, anxiety disorders, a phobic disorder, a learning disorder, a memory disorder, amnesia, age-related memory loss, attention deficit disorder, dysthymic disorder, major depressive disorder, mania, obsessive-compulsive disorder, psychoactive substance use disorders, anxiety, panic disorder, bipolar affective disorder, BP-1, migraine, traumatic brain injury, spinal cord trauma, motor neuron disease, or nerve damage.

30. The method of claim 1, wherein said disease is cancer.

31. The method of claim 30, wherein said cancer is a tumor.

32. The method of claim 30, wherein said tetracycline compound inhibits tumor metastasis.

33. The method of claim 31, wherein said tumor is a carcinoma or a sarcoma.

34. The method of claim 30, wherein said tetracycline compound decreases angiogenesis.

35. The method of any one of claims 1, 2, 28, or 30, wherein said tetracycline compound is administered in combination with a second agent.

36. The method of claim 35, wherein said second agent is a chemotherapeutic agent or radiation therapy.

37. The method of claim 35, wherein said second agent is a neuroprotective agent.

38. The method of claim 37, wherein said neuroprotective agent comprises a compound that remove protein build up, anti-inflammatory agents, omega-3 fatty acids, minocycline, dexanabionol, compounds that increase energy available to cells, anti-oxidants, gingko biloba, co-enzyme Q-10, vitamin E, vitamin C, vitamin A, selenium, lipoic acid, selegine, anti-glutamate therapies, remacemide, riluzole, lamotrigine, gabapentin, GABA-ergic therapies baclofen, muscimol, gene transcription regulator, glucocorticoids, retinoic acid, erythropoietin, TNF-α antagonists, cholinesterase inhibitors, N-methyl-D-aspartate (NMDA) antagonists, opiod antagonists, neuronal membrane stabilizers, CDP-choline, calcium channel blockers, sodium channel blockers, or prednisone.

39. The method of claim 35, wherein said second agent is an antiinfective agent.

40. The method of claim 1, wherein said tetracycline compound is administered with a suitable pharmaceutical carrier.

41. The method of claim 1, wherein said subject is a human.

42. The method of claim 2 or 3, wherein said inflammation process associated state is associated with activation of immune related cells.

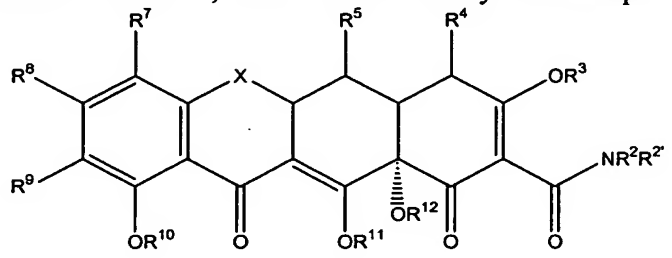
43. The method of claim 42, wherein said activation of immune related cells comprises the production of inflammatory factors.

44. The method of claim 42, wherein said activation of immune related cell types comprises adhesion of cells.

45. The method of claim 42, wherein said activation of immune related cell types comprises migration of cells.

46. The method of claim 2, wherein said inflammatory process associated state is a mitochondrial associated state.

47. The method of claim 1, wherein said tetracycline compound is of formula I:



(I)

wherein

R^2, $R^{2'}$, $R^{4'}$, and $R^{4''}$ are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^{2'}$, R^3, R^{10}, R^{11} and R^{12} are are each independently hydrogen, alkyl, aryl, benzyl, arylalkyl, or a pro-drug moiety;

R^4 is $NR^{4'}R^{4''}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R^5 is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{9f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;
E' is O, NR^{8f}, or S;
W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;
W' is O, NR^{7f}, or S;
X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^{6}$, S, NR^{6}, or O;
Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;
Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;
Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

48. The method of claim 47, wherein R^2, $R^{2'}$, R^8, R^{10}, R^{11}, and R^{12} are each hydrogen, X is $CR^6R^{6'}$, and R^4 is $NR^{4'}R^{4''}$, wherein $R^{4'}$ and $R^{4''}$ are each methyl.

49. The method of claim 48, wherein R^9 is hydrogen.

50. The method of claim 49, wherein R^7 is substituted or unsubstituted aryl.

51. The method of claim 50, wherein said aryl is substituted with an amino group.

52. The method of claim 49, wherein R^7 is a substituted or unsubstituted heterocycle.

53. The method of claim 52, wherein said heterocycle is substituted with an amino group.

54. The method of claim 49, wherein R^7 is substituted or unsubstituted alkenyl.

55. The method of claim 49, wherein R^7 is substituted or unsubstituted alkynyl.

56. The method of claim 49, wherein R^7 is substituted or unsubstituted alkyl.

57. The method of claim 56, wherein R^7 is substituted with an aryl group.

58. The method of claim 56, wherein R^7 is substituted with a carbonyl group.

59. The method of claim 56, wherein R^7 is substituted with an amino group.

60. The method of claim 59, wherein said amino group is alkylamino.

61. The method of claim 49, wherein R^7 is $-CH_2NR^{7c}C(=W')WR^{7a}$.

62. The method of claim 61, wherein R^{7c} is hydrogen, and W and W' are each oxygen.

63. The method of claim 49, wherein R^7 is $-NR^{7c}C(=W')WR^{7a}$.

64. The method of claim 63, wherein R^{7c} is hydrogen, and W and W' are each oxygen.

65. The method of claim 49, wherein R^7 is substituted or unsubstituted acyl.

66. The method of claim 49, wherein R^7 is substituted or unsubstituted amino.

67. The method of claim 49, wherein R^7 is substituted or unsubstituted oximyl.

68. The method of claim 49, wherein R^7 is hydrogen or dimethylamino.

69. The method of claim 68, wherein R^9 is substituted or unsubstituted amino.

70. The method of claim 69, wherein said amino is alkylamino.

71. The method of claim 68, wherein R^9 is substituted or unsubstituted alkyl.

72. The method of claim 71, wherein said substituted alkyl is substituted with an substituted or unsubstituted amino or amido group.

73. The method of claim 72, wherein said amino group is substituted or unsubstituted alkylamino.

74. The method of claim 68, wherein R^9 is substituted or unsubstituted aryl.

75. The method of claim 74, wherein said aryl group is substituted or unsubstituted phenyl.

76. The method of claim 75, wherein said phenyl group is substituted with amino.

77. The method of claim 68, wherein R^9 is a substituted or unsubstituted heterocycle.

78. The method of claim 68, wherein R^9 is substituted or unsubstituted alkynyl.

79. The method of claim 68, wherein R^9 is $-CH_2NR^{9c}C(=Z')ZR^{9a}$.

80. The method of claim 79, wherein R^{9c} is hydrogen, Z' is oxygen and Z is nitrogen.

81. The method of claim 79, wherein R^{9c} is hydrogen, Z' and Z are oxygen.

82. The method of claim 78, wherein R^9 is $-NR^{9c}C(=Z')ZR^{9a}$.

83. The method of claim 82, wherein R^{9c} is hydrogen, Z' is oxygen and Z is nitrogen.

84. The method of claim 48, wherein R^9 is substituted or unsubstituted alkyl.

85. The method of claim 84, wherein R^9 is substituted with amino.

86. The method of claim 85, wherein R^9 is substituted or unsubstituted alkylaminoalkyl.

87. The method of claim 84 or 85, wherein R^7 is substituted or unsubstituted alkyl.

88. The method of claim 87, wherein R^7 is substituted with amino.

89. The method of claim 84, wherein R^7 is substituted or unsubstituted alkynyl.

90. The method of claim 86, wherein R^7 is a substituted or unsubstituted heterocycle.

91. The method of claim 48, wherein R^7 is substituted or unsubstituted alkyl.

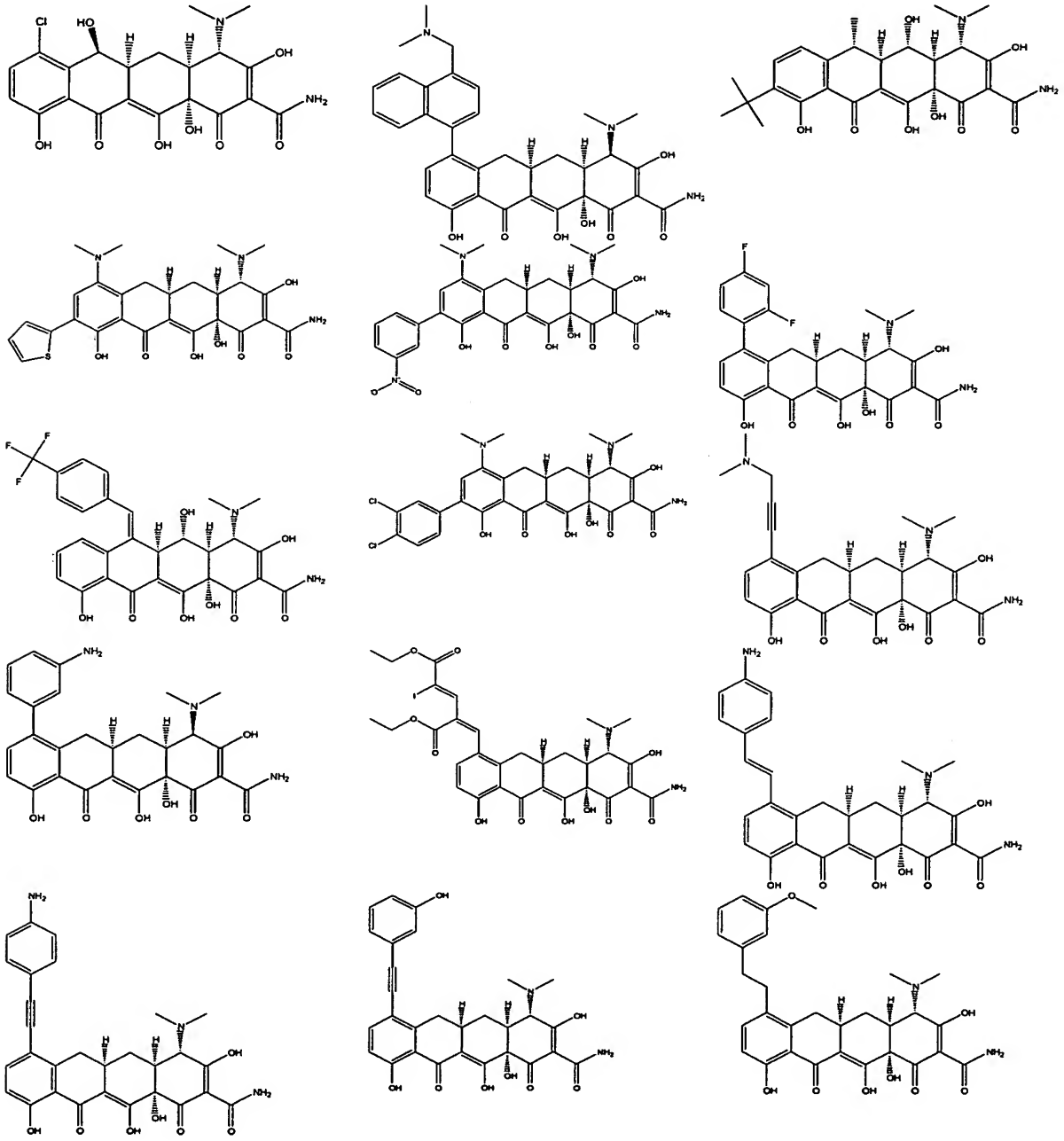
92. The method of claim 91, wherein R^7 is substituted with substituted or unsubstituted amino.

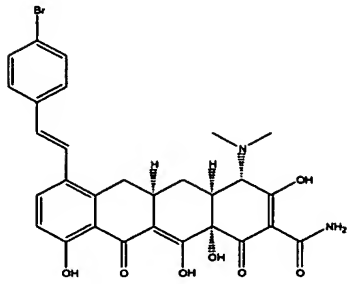
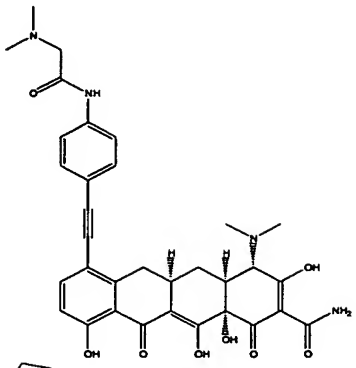
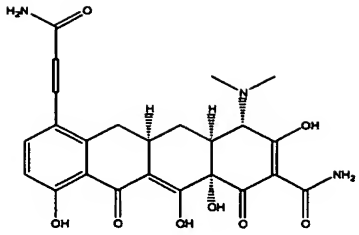
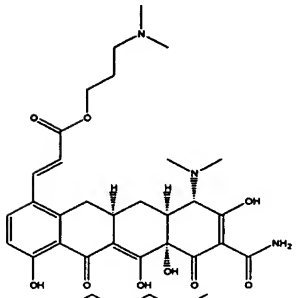
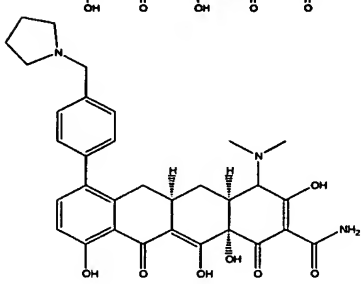
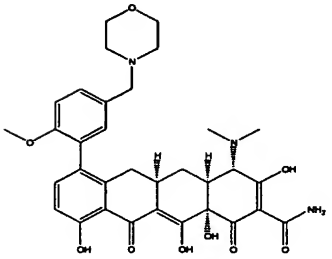
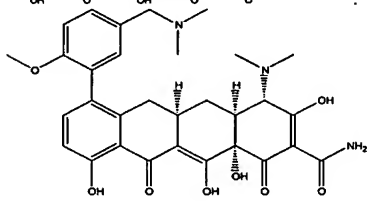
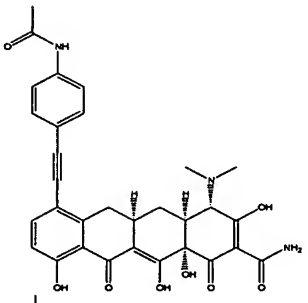
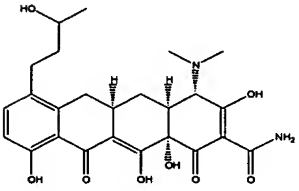
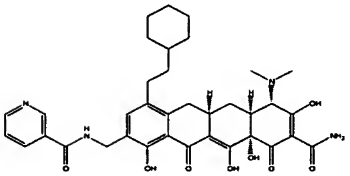
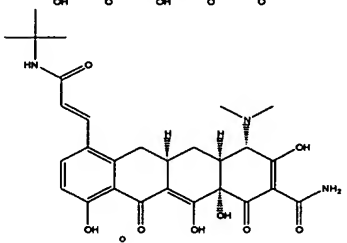
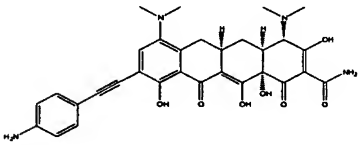
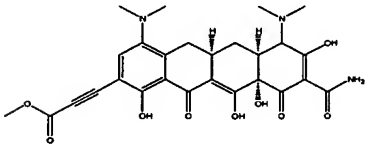
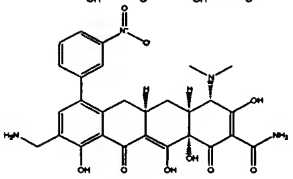
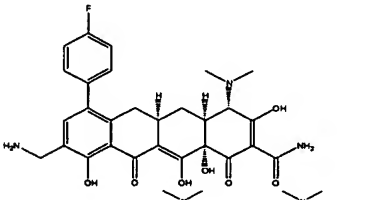
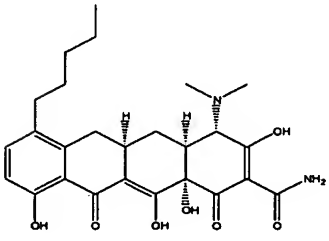
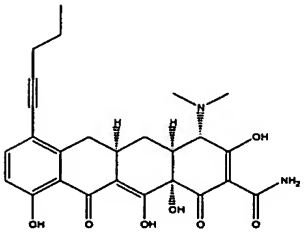
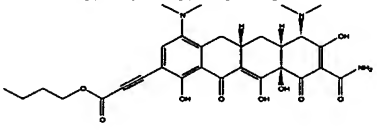
93. The method of claim 92, wherein R^9 is $-NR^{9c}C(=Z')ZR^{9a}$, R^{9c} is hydrogen, Z' is oxygen and Z is oxygen.

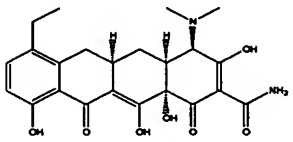
94. The method of claim 48, wherein X is $C=CR^{13}Y$, R^{13} is aryl and Y is hydrogen.

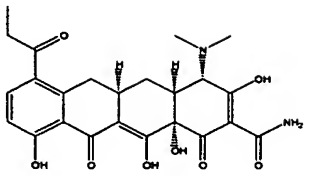
95. The method of claim 47, wherein R^7 is a dimeric moiety.

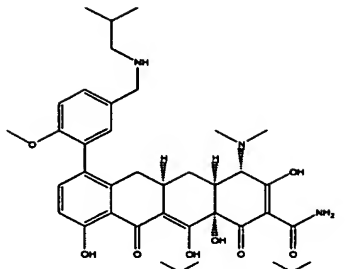
96. The method of claim 47, wherein said tetracycline compound is selected from the group consisting of:

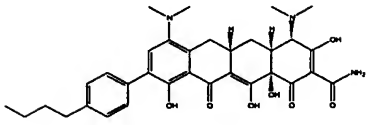


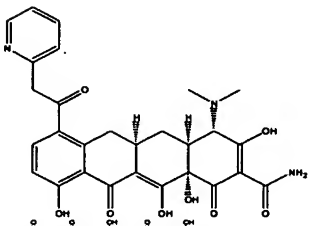



















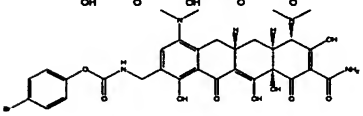


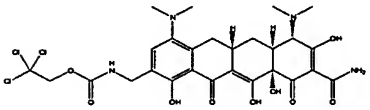


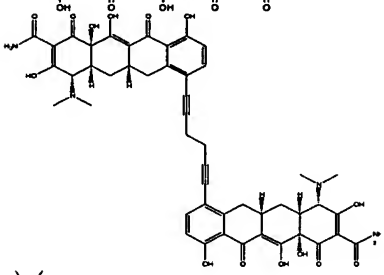


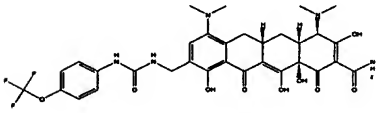


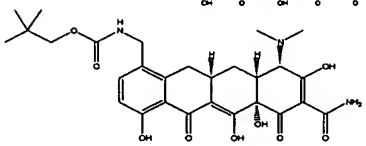


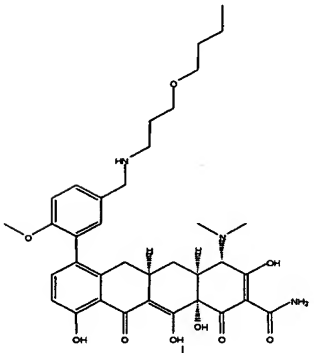


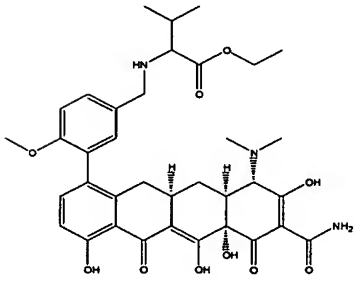


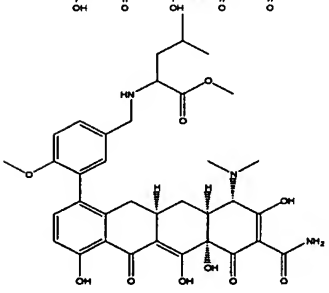


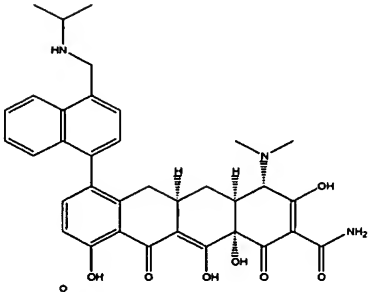


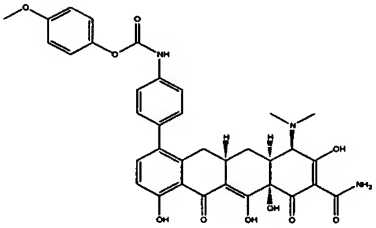


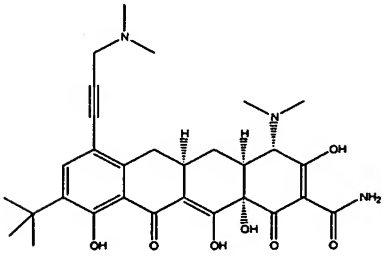


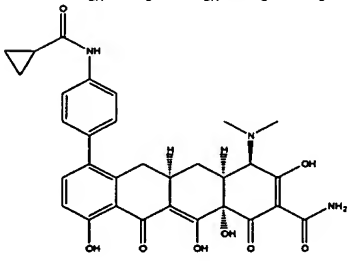


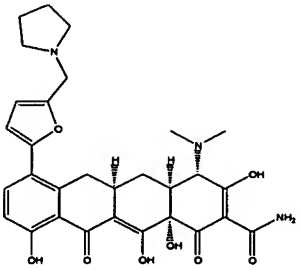


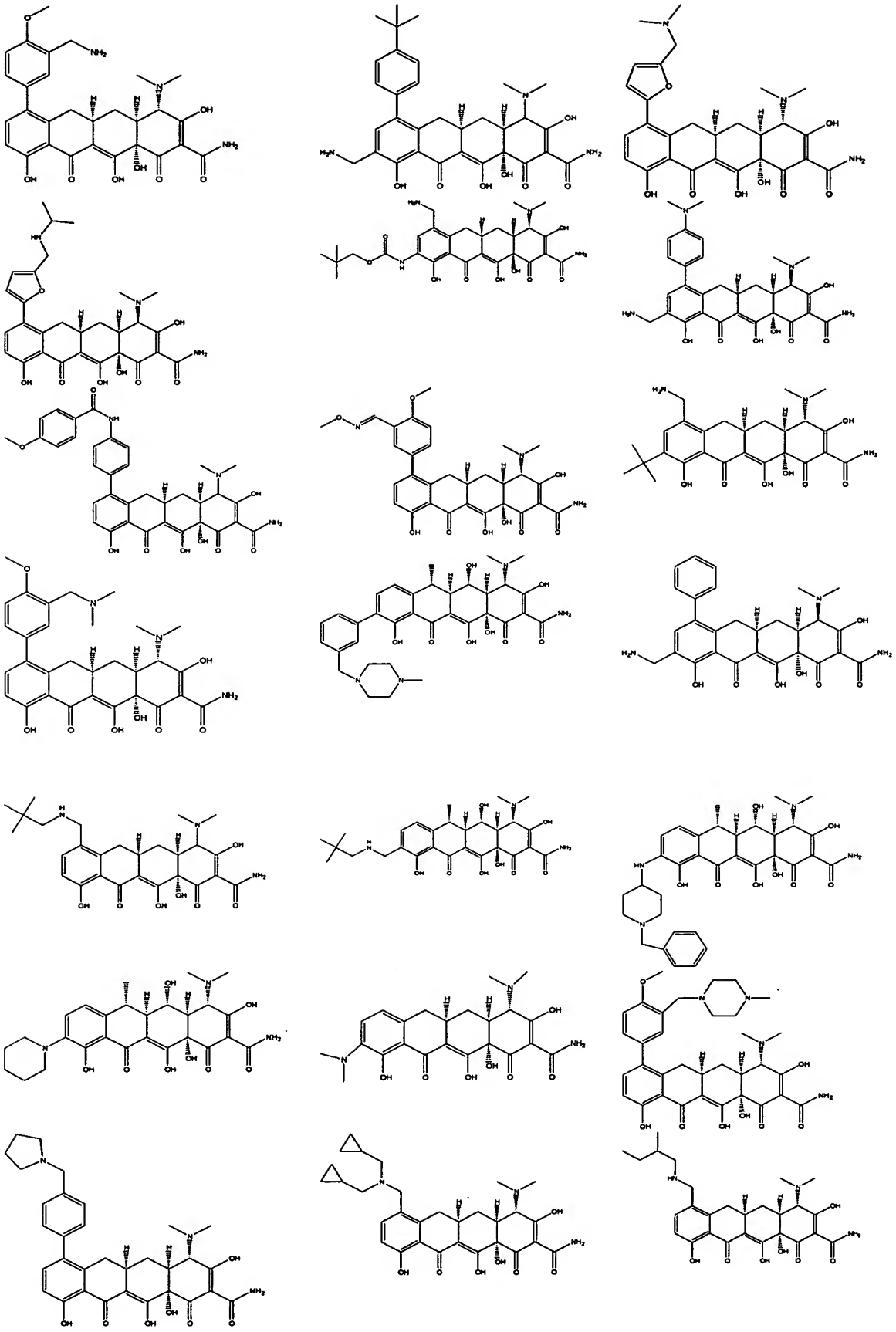


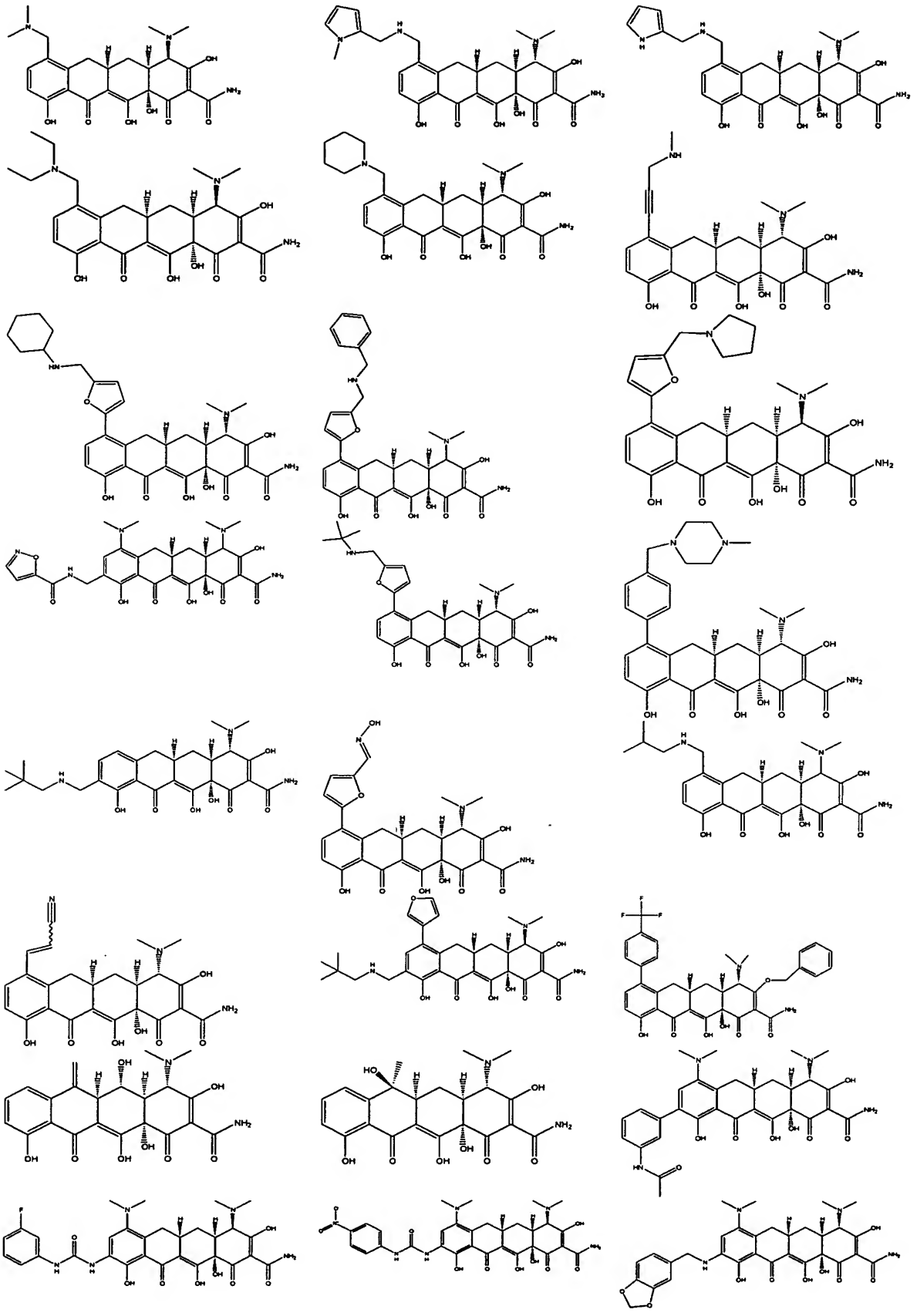


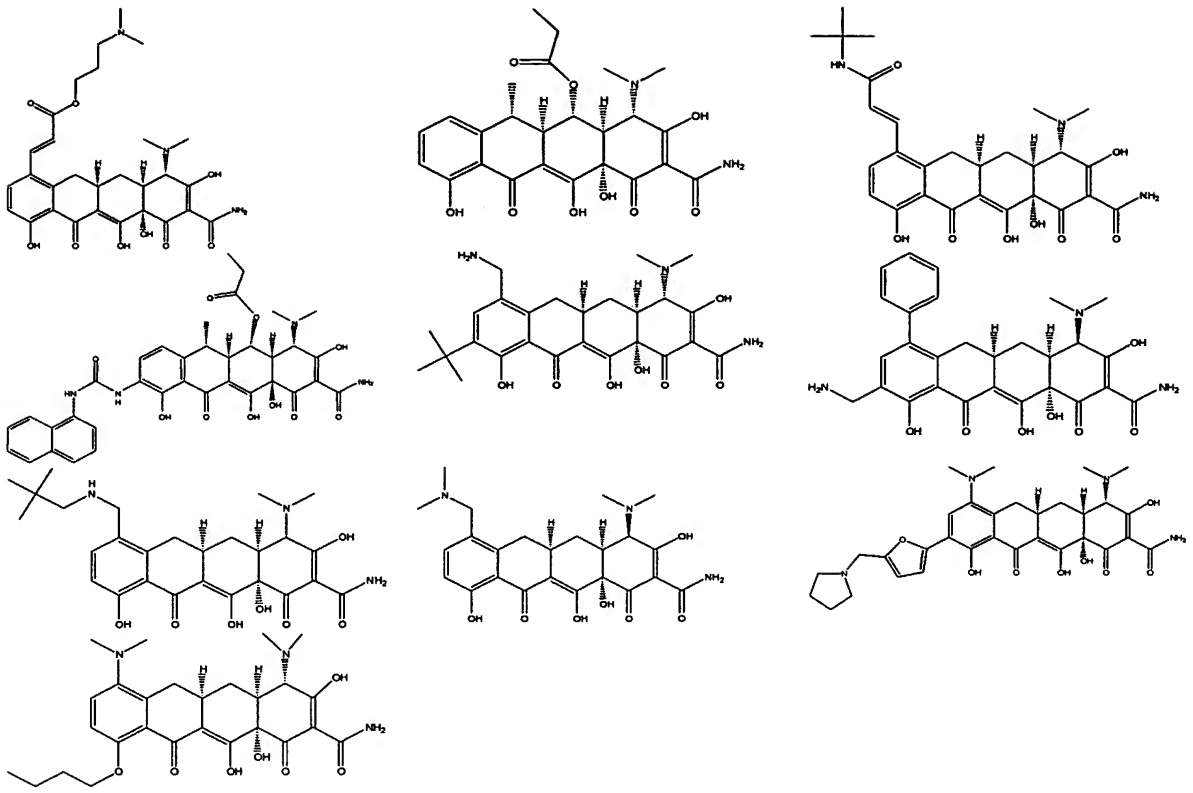








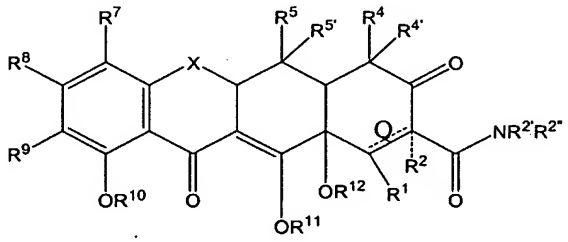




97. The method of claim 1, wherein said tetracycline compound is a compound of Table 2, Table 3, or Table 4.

98. The method of claim 47, wherein R^{10} is alkyl.

99. The method of claim 1, wherein said tetracycline compound is of the formula (II):



(II)

wherein

R^1 is hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, amido, alkylamino, amino, arylamino, alkylcarbonyl, arylcarbonyl, alkylaminocarbonyl, alkoxy, alkoxycarbonyl, alkylcarbonyloxy, alkyloxycarbonyloxy, arylcarbonyloxy, aryloxy, thiol, alkylthio, arylthio, alkenyl, heterocyclic, hydroxy, or halogen, optionally linked to R^2 to form a ring;

R^2 is hydrogen, alkyl, halogen, hydroxyl, thiol, alkenyl, alkynyl, aryl, acyl, formyl, cyano, nitro, alkoxy, amino, alkylamino, heterocyclic, or absent, optionally linked to R^1 to form a ring;

$R^{2'}$, $R^{2''}$, R^{4a}, and R^{4b} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{10}, R^{11} and R^{12} are each independently hydrogen, alkyl, aryl, benzyl, arylalkyl, or a pro-drug moiety;

R^4 and $R^{4'}$ are each independently $NR^{4a}R^{4b}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R^5 and $R^{5'}$ are each independently hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{9f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;

E' is O, NR^{8f}, or S;

Q is a double bond when R^2 is absent, Q is a single bond when R^2 is hydrogen, alkyl, halogen, hydroxyl, thiol, alkenyl, alkynyl, aryl, acyl, formyl, cyano, nitro, alkoxy, amino, alkylamino, or heterocyclic;

W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;

W' is O, NR^{7f}, or S;

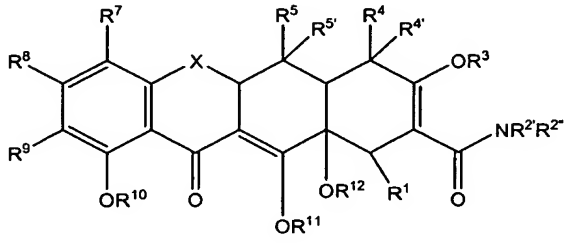
X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^{6}$, S, NR^{6}, or O;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;

Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

100. The method of claim 1, wherein said tetracycline compound is of the formula (III):



(III)

wherein

R^{1} is hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, amido, alkylamino, amino, arylamino, alkylcarbonyl, arylcarbonyl, alkylaminocarbonyl, alkoxy, alkoxycarbonyl, alkylcarbonyloxy, alkyloxycarbonyloxy, arylcarbonyloxy, aryloxy, thiol, alkylthio, arylthio, alkenyl, heterocyclic, hydroxy, or halogen;

$R^{2'}$, $R^{2"}$, R^{4a}, and R^{4b} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{3}, R^{10}, R^{11} and R^{12} are each independently hydrogen, alkyl, aryl, benzyl, arylalkyl, or a pro-drug moiety;

R^{4} and $R^{4'}$ are each independently $NR^{4a}R^{4b}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R^{5} and $R^{5'}$ are each independently hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^{6} and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{9f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;

E' is O, NR^{8f}, or S;

W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;

W' is O, NR^{7f}, or S;

X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^6$, S, NR^6, or O;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;

Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

101. The method of claim 99, wherein Q is a double bond and R^1 is hydrogen.

102. The method of claim 100, wherein R^1 is alkyl amino.

103. The method of claim 1, wherein said tetracycline has antibacterial activity.

104. The method of claim 1, wherein said tetracycline compound is a 2, 3, 5, 7, 9, and/or 10, substituted tetracycline compound.

105. The method of claim 1, wherein said tetracycline compound is anti-infective.

106. The method of claim 1, wherein said tetracycline compound is not anti-infective.

107. The method of claim 1, wherein said tetracycline compound is administered with a suitable pharmaceutical carrier.

108. The method of claim 1, wherein said subject is a human.

109. A pharmaceutical composition comprising an effective amount of a tetracycline compound in combination with a second agent, wherein said tetracycline compound has a target therapeutic activity.

110. The pharmaceutical composition of claim 109, wherein said tetracycline compound is a substituted tetracycline compound.

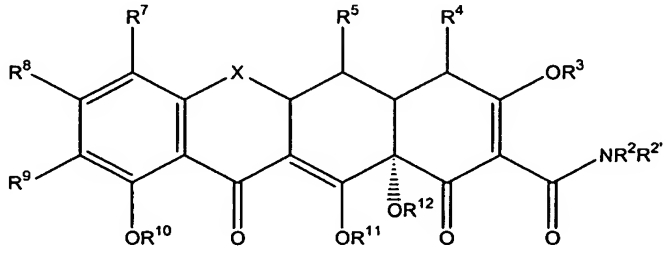
111. The pharmaceutical composition of claim 109, wherein said second agent is a neuroprotective agent.

112. The pharmaceutical composition of claim 109, wherein said second agent is a chemotherapeutic agent.

113. The pharmaceutical composition of claim 109, wherein said second agent is an antiinfective agent.

114. The pharmaceutical composition of claim 113, wherein said antiinfective agent is an antibacterial, antifungal, antiparasitic or antiviral agent.

115. The pharmaceutical compositions of claim 109, wherein said tetracycline compound is of the formula (I):



(I)

wherein

R^2, $R^{2'}$, $R^{4'}$, and $R^{4''}$ are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

$R^{2'}$, R^3, R^{10}, R^{11} and R^{12} are are each independently hydrogen, alkyl, aryl, benzyl, arylalkyl, or a pro-drug moiety;

R^4 is $NR^{4'}R^{4''}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R^5 is hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{9f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;

E' is O, NR^{8f}, or S;

W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;

W' is O, NR^{7f}, or S;

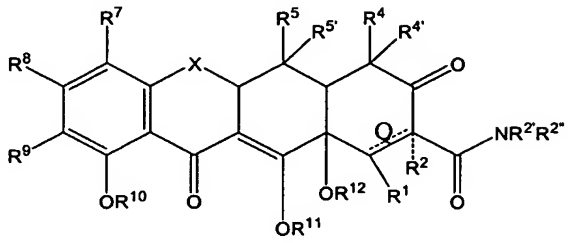
X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^6$, S, NR^6, or O;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;

Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

116. The pharmaceutical compositions of claim 109, wherein said tetracycline compound is of the formula (II):



(II)

wherein

R^1 is hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, amido, alkylamino, amino, arylamino, alkylcarbonyl, arylcarbonyl, alkylaminocarbonyl, alkoxy, alkoxycarbonyl, alkylcarbonyloxy, alkyloxycarbonyloxy, arylcarbonyloxy, aryloxy, thiol, alkylthio, arylthio, alkenyl, heterocyclic, hydroxy, or halogen, optionally linked to R^2 to form a ring;

R^2 is hydrogen, alkyl, halogen, hydroxyl, thiol, alkenyl, alkynyl, aryl, acyl, formyl, cyano, nitro, alkoxy, amino, alkylamino, heterocyclic, or absent, optionally linked to R^1 to form a ring;

$R^{2'}$, $R^{2''}$, R^{4a}, and R^{4b} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{10}, R^{11} and R^{12} are each independently hydrogen, alkyl, aryl, benzyl, arylalkyl, or a pro-drug moiety;

R^4 and $R^{4'}$ are each independently $NR^{4a}R^{4b}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R^5 and $R^{5'}$ are each independently hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{9f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;

E' is O, NR^{8f}, or S;

Q is a double bond when R^2 is absent, Q is a single bond when R^2 is hydrogen, alkyl, halogen, hydroxyl, thiol, alkenyl, alkynyl, aryl, acyl, formyl, cyano, nitro, alkoxy, amino, alkylamino, or heterocyclic;

W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;

W' is O, NR^{7f}, or S;

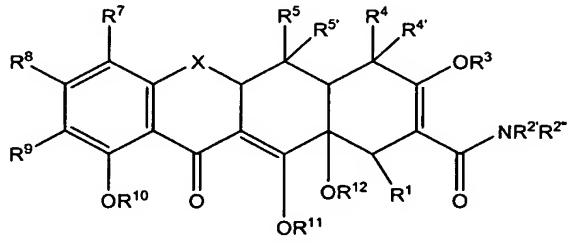
X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^6$, S, NR^6, or O;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;

Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

117. The pharmaceutical compositions of claim 109, wherein said tetracycline compound is of the formula (III):



(III)

wherein

R^1 is hydrogen, alkyl, alkenyl, alkynyl, aryl, arylalkyl, amido, alkylamino, amino, arylamino, alkylcarbonyl, arylcarbonyl, alkylaminocarbonyl, alkoxy, alkoxycarbonyl, alkylcarbonyloxy, alkyloxycarbonyloxy, arylcarbonyloxy, aryloxy, thiol, alkylthio, arylthio, alkenyl, heterocyclic, hydroxy, or halogen;

$R^{2'}$, $R^{2''}$, R^{4a}, and R^{4b} are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^3, R^{10}, R^{11} and R^{12} are each independently hydrogen, alkyl, aryl, benzyl, arylalkyl, or a pro-drug moiety;

R^4 and $R^{4'}$ are each independently $NR^{4a}R^{4b}$, alkyl, alkenyl, alkynyl, hydroxyl, halogen, or hydrogen;

R^5 and $R^{5'}$ are each independently hydroxyl, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, alkyl carbonyloxy, or aryl carbonyloxy;

R^6 and $R^{6'}$ are each independently hydrogen, methylene, absent, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R^7 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{7c}C(=W')WR^{7a}$;

R^8 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{8c}C(=E')ER^{8a}$;

R^9 is hydrogen, hydroxyl, halogen, thiol, nitro, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, arylalkyl, amino, arylalkenyl, arylalkynyl, acyl, aminoalkyl, heterocyclic, thionitroso, or $-(CH_2)_{0-3}NR^{9c}C(=Z')ZR^{9a}$;

R^{7a}, R^{7b}, R^{7c}, R^{7d}, R^{7e}, R^{7f}, R^{8a}, R^{8b}, R^{8c}, R^{8d}, R^{8e}, R^{8f}, R^{9a}, R^{9b}, R^{9c}, R^{9d}, R^{9e}, and R^{9f} are each independently hydrogen, acyl, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety;

R^{13} is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

E is $CR^{8d}R^{8e}$, S, NR^{8b} or O;

E' is O, NR^{8f}, or S;

W is $CR^{7d}R^{7e}$, S, NR^{7b} or O;

W' is O, NR^{7f}, or S;

X is $CHC(R^{13}Y'Y)$, $C{=}CR^{13}Y$, $CR^{6'}R^6$, S, NR^6, or O;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Z is $CR^{9d}R^{9e}$, S, NR^{9b} or O;

Z' is O, S, or NR^{9f}, and pharmaceutically acceptable salts, esters and enantiomers thereof.

118. The pharmaceutical composition of claim 109, wherein said tetracycline compound is a compound of Table 2, or Table 4.

119. The pharmaceutical composition of claim 109, wherein said tetracycline compound is a compound of Table 3.

120. The pharmaceutical composition of claim 109, wherein said pharmaceutical composition further comprises a pharmaceutically acceptable carrier.

121. The pharmaceutical composition of claim 109, wherein said effective amount is effective to treat cancer.

122. The pharmaceutical composition of claim 121, wherein said effective amount is effective to treat a neurological disorder.

123. A packaged composition for treatment of a disease with a tetracycline compound with a target therapeutic activity, comprising a tetracycline compound having said target therapeutic activity and directions for using said tetracycline compound for treating said disease.

124. The packaged composition of claim 123, further comprising a pharmaceutically acceptable carrier.

125. The packaged composition of claim 123, wherein said disease is an IPAS.

126. The packaged composition of claim 123, wherein said disease is a neurological disorder.

127. The packaged composition of claim 123, wherein said disease is cancer.

128. The packaged composition of claim 123, wherein said tetracycline compound is a substituted tetracycline compound.

129. The packaged composition of claim 123, further comprising a second agent.

130. The packaged composition of claim 129, wherein said second agent is a chemotherapeutic agent.

131. The packaged composition of claim 129, wherein said second agent is an antiinfective agent.

132. The packaged composition of claim 129, wherein said second agent is an neuroprotective agent.